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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,923	09/18/2003	Alphonse Galdes	WYTH-P03-069	1889

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EXAMINER	
BRANNOCK, MICHAEL T	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 10/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/665,923	GALDES ET AL.	
	Examiner	Art Unit	
	Michael Brannock	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *7,8,14 and 17-19, 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,9-13,15,16 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *091803*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application: Claims and Amendments

Applicant is notified that the amendments put forth on 9/18/2003, have been entered in full.

Claims 1-21 are pending. Claims 7, 8, 14, 17-19 and 21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 7/24/2006.

Applicants election of Group I, as the claims to in vivo methods of promoting survival of neurons in Parkinson's disease, i.e. striatial dopamine neurons, by administering a palmitoylated hedgehog protein, is acknowledged. Applicant asserts that claims 1-6 and 9-16 read on the elected invention. However, the examiner believes that claim 14 does not encompass the palmitoyl moiety. The traversal is on the grounds that a search of the groups would not be a serious burden on the examiner. This is not found persuasive for the following reasons:

Under MPEP § 803, there are two criteria for a proper requirement for restriction between patentably distinct inventions:

(A) The inventions must be independent (see MPEP § 8702.01, 806.04, 808.01) **or** distinct as claimed (see MPEP § 806.05- §806.05(I)): and

(B) There must be a serious burden on the examiner if restriction is required (see MPEP § 803.02, § 806.04(a)- 806.04(I), § 808.01(a), and § 808.02).

Consistent with current patent practice, a serious search burden may be established by (A) separate classification thereof: (B) a separate status in the art when they are classifiable

together: (C) a different field of search. These criteria were met in the above restriction. Further, a search is directed not only to art which would be anticipatory, but also to art that would render the invention obvious. In the instant case, the two method groups are considered patentably distinct because the two methods require substantially different consideration based upon the location and circumstances of treatment. For example, the modulating *in vivo* activity of a particular product requires consideration of the medical condition which would necessitate such treatment, efficacy (e.g. route of administration, dosage amounts, possible interactions with other body compounds and physiological systems) and ability to reach the cellular target. Such considerations are not required for the analysis of methods for product modulating activity in a defined *in vitro* environment, which requires separate considerations with regard to obviousness and enablement including media determination, substrate, and other conditions for growth of target cells and use of the claimed method in culture. The two inventions, therefore, are patentably distinct and although a search of one may overlap that of the other, the search of one could not be relied upon, solely, to provide art that is anticipatory or would render obvious the invention of the other, and to search both inventions would be burdensome.

Claim Objections

Claim 9 is objected to because of the following informalities: sterol is spelled incorrectly. Appropriate correction is required.

Information Disclosure Statement

The information disclosure statement filed 9/18/2003 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP 609 because citations CK and CT lack sufficient description so as to lead the reader to the cited documents. The documents provided have not been considered and the citations will not be printed. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP 609 C(1).

Sequence Rules Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reasons: The specification makes reference to specific polynucleotide and/or polypeptide sequences, see page 49 for example; these references must contain a sequence identifier of the form: SEQ ID NO: X. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 9 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Miao et al., J. Neuroscience, August 1, 1997, 17(15)5891-5899.

Miao et al. disclose that sonic hedgehog polypeptides promotes the survival of post-induction midbrain Dopaminergic and GABAergic neurons *in vitro* (see the Abstract). Further, the sonic hedgehog polypeptides used by Miao et al. were produced using the Baculovirus expression system which was known at the time to produce a lipophilic cholesterol conjugated sonic hedgehog (see Materials and Methods, and references therein).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6, 9-13, 15, 16, 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miao et al., J. Neuroscience, August 1, 1997, 17(15)5891-5899 in view of Pepinsky-RB et al., JBC 273(22)14037-14045, May 29, 1998.

Miao et al. disclose that sonic hedgehog polypeptides promotes the survival of post-induction midbrain Dopaminergic and GABAergic neurons *in vitro* (see the Abstract), such cell types being well known to be lost in Parkinson's and Huntington's disease, respectively. Further, the sonic hedgehog polypeptides used by Miao et al. were produced using the Baculovirus expression system which was known at the time to produce a lipophilic cholesterol conjugated sonic hedgehog (see Materials and Methods, and references therein). Further, Miao et al. disclose that significant levels of sonic hedgehog protein are found in the adult central nervous system, particularly the substantia nigra (see page 5898, first paragraph). Miao et. al. do not report the actual treatment of a patient with sonic hedgehog polypeptides. However, based on the evidence obtained, Miao et al. conclude that sonic hedgehog may have value as a protective agent in neurodegenerative disease (see the Abstract). Further, one of ordinary skill in the art would appreciate that the neurodegenerative diseases Miao et al. referred to are Parkinson's disease and Huntington's disease, based on the well known associations of these diseases with the cell types studied by Miao et al. Additionally, Miao et al., were not aware that palmitoylated hedgehog proteins were up to 30 times more potent than those without. Pepinsky RB *et al.* teaches that that palmitoylation of hedgehog increased the potency of hedgehog by about 30 percent (see the Abstract).

Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made, with reasonable expectation of success, to treat diseases characterized by a

loss of Dopaminergic and/or GABAergic neurons, e.g. Parkinson's Disease and Huntington's Disease, by administering sonic hedgehog, as taught by Miao et al. and as modified by Pepinsky et al. The motivation to do so was provided by Miao et al., who stated that Sonic Hedgehog promotes the survival of post-induction midbrain Dopaminergic and GABAergic neurons (see the Abstract), and particularly protects cultures of Midbrain dopminergic neurons from the toxic effects of MPP+, a specific neurotoxin that induces Parkinsonism *in vivo* (see page 5891, col 2) and by Pepinsky RB *et al.* who stated that palmitoylation of hedgehog increased the potency of hedgehog by about 30 percent (see the Abstract).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-69-13, 15, 16, 20 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No: 6897297.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

U.S. Patent No: 6897297 discloses that hydrophobically-modified hedgehog proteins of the invention are also useful in gene therapy methods. For neurodegenerative disorders, several animal models are available that are believed to have some clinical predicative value. For Parkinson's disease, models involve the protection, or the recovery in rodents or primates in which the nigral-striatal dopaminergic pathway is damaged either by the systemic administration of MPTP or the local (intracranial) administration of 6-hydroxydopamine [6-OHDA], two selective dopaminergic toxins. Specific models are: MPTP-treated mouse model (64); MPTP-treated primate (marmoset or Rhesus) model (65), and the unilateral 6-OHDA lesion rat model (66). Preferred modifications to the hedgehog polypeptide include, palmitoyl [148] and cholesterol moieties [163].

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 6, 9-13 require a method of preventing Parkinson's disease. However, the term "preventing", given its broadest reasonable interpretation with the specification, requires that absolutely no cell, nor tissue, would present any symptom of a disorder after treatment with the hedgehog polypeptides. There is no evidence, either in the specification nor in the prior art, that any method to date can accomplish this goal. The specification presents the results of an experiment demonstrating that exogenous application of hedgehog can protect from neuropathy in rats, however there is no support for the prevention of any disorder, as is required by the claims, and neither can such support be obtained through reasonable extrapolation of the data.

Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D., can be reached at (571) 272-0867. Official papers filed by fax should be directed to **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER

October 14, 2006